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CASE REPORT

Squamous cell carcinoma of the ovary arising from a mature cystic teratoma associated with hypercalcaemia

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Abstract

We present a rare case of a 40-year-old nulliparous lady, with no past medical or surgical history, who was diagnosed with metastatic squamous cell carcinoma of the right ovary that originated from a mature cystic ovarian teratoma. Our patient underwent debulking total abdominal hysterectomy, bilateral salpingo-oophorectomy and partial omentectomy followed by postoperative carboplatin and paclitaxel chemotherapy. Rapid disease progression ensued, complicated by severe parathyroid hormone-related protein-induced hypercalcaemia resistant to medical therapy. The patient was treated in a palliative manner and died five months after her diagnosis.

Key words: Teratoma; Carcinoma; Squamous cell; Hypercalcaemia; Parathyroid hormone related-protein

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Introduction

Hypercalcaemia has been previously associated with gynaecologic malignant neoplasms such as those originating from the ovary, uterus, vulva, and vagina but only infrequently with a squamous cell carcinoma (SCC) arising in a mature cystic teratoma (MCT). We report a case of a young lady diagnosed with an SCC arising from an MCT associated with humoral hypercalcaemia of malignancy.

Case report

A 40-year-old lady presented with a month's history of progressively worsening left flank and lower abdominal pain associated with urinary frequency and urgency. Clinical examination revealed a large mass occupying the abdomen and rising to the umbilicus.

A pelvic magnetic resonance imaging (MRI) showed a 4.5 × 2 cm fat-containing dermoid cyst with benign imaging characteristics, arising from the lateral border of the right ovary. A 9.6 × 7.5 × 8.5 cm dermoid cyst containing fat and soft tissue arose from the lateral border of the left ovary. Arising from the cranial pole of the left cyst was a 6 × 2.3 × 3 cm mass lesion with contour lobulation and irregular contrast enhancement. Originating from its inferior and medial aspect was a 10.7 × 8.5 × 12 cm necrotic tumour mass with peripheral contrast enhancement and associated restricted diffusion (Figures 1,2).

Tumour markers including alpha fetoprotein (AFP), human chorionic gonadotropin (HCG), cancer antigen 125 (CA 125), lactate dehydrogenase (LDH), carcinoembryonic antigen (CEA) were normal. Cancer antigen 19.9 (CA19.9) was raised at 29.2 (0–2.5 ng/mL). Total abdominal hysterectomy and right salpingo-oophorectomy resected the right ovary, but the left ovarian mass infiltrated the bladder dome, the posterior wall of the bladder, and the area of the right ureteric orifice. Extensive debulking was performed with less than 2 cm of disease remaining *in situ*.

Histology revealed mature cystic teratoma of the right ovary with an area of dysplastic squamous epithelium adjacent to a large keratinising moderately differentiated squamous cell carcinoma. The left ovary showed mature cystic teratoma with a tumour deposit of squamous cell carcinoma on the surface of the left adnexa. Diagnosis of Grade II squamous cell carcinoma of the right ovary arising in a mature cystic teratoma with extension beyond the ovarian capsule with metastatic spread to the left adnexa was made.

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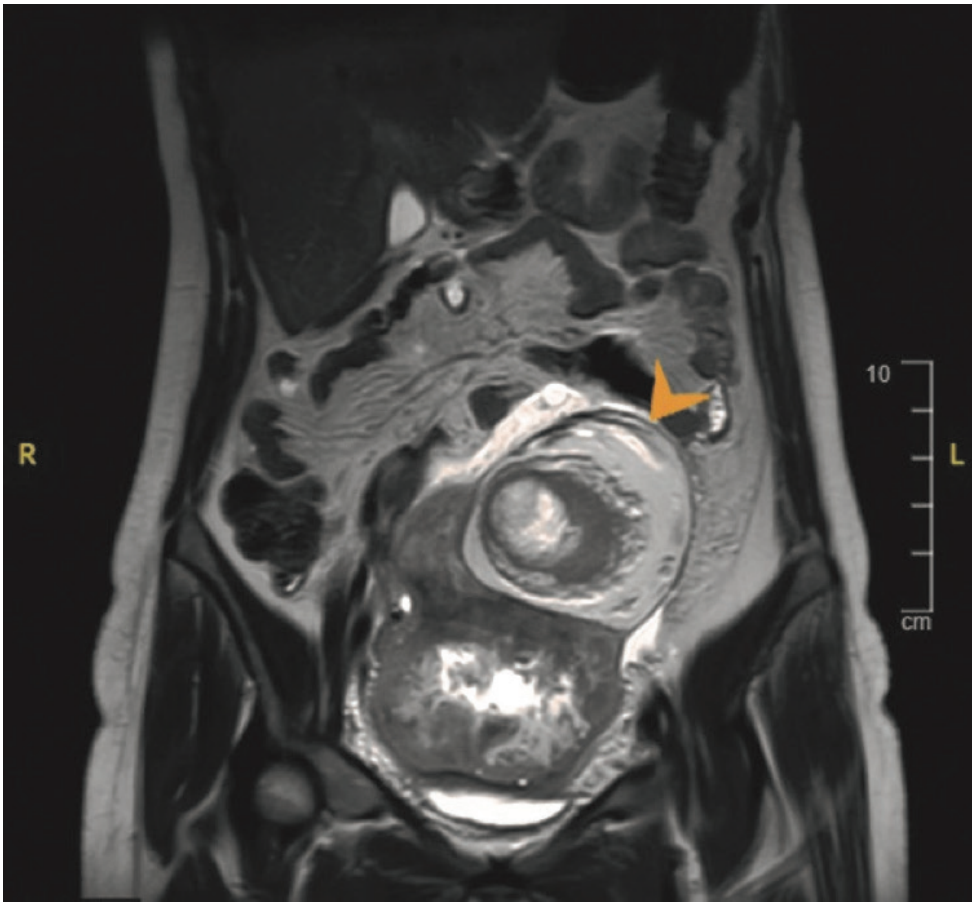

Figure 1. Coronal view of MR pelvis showing pelvic mass (arrow pointing to mass originating from the cranial pole of the left lesion). MR, magnetic resonance; R, right; L, left.

She underwent 5 cycles of carboplatin and paclitaxel chemotherapy. She developed humoral hypercalcaemia of malignancy as evidenced by the investigations in **Table 1**. This was treated with intravenous 0.9% saline 1 litre 12 hourly. She developed lethargy, poor appetite, confusion, and pain managed with continuous intravenous fluid replacement and one dose of 4 mg Zoledronic acid IV (**Figure 3**).

A Computed tomography scan of the pelvis to assess treatment response showed an abscess within an 11.8 × 11.6 × 9 cm tumour mass invading the abdominal wall. Chemotherapy was not restarted, and the intent of treatment changed to best supportive care given disease progression, ongoing infection, and poor performance status. She died 2 months after her last chemotherapy treatment.

Discussion

Mature cystic teratoma (MCT) is a common germ cell neoplasm of the ovary. Malignant transformation occurs in 1.5%–2% of cases, usually observed in post-menopausal females (Maharjan, 2019). The mean age for squamous cell carcinoma (SCC) in an MCT is 55 years. The mean size for malignant tumours is 152 mm vs 88 mm for benign tumours (Patni, 2014).

80% of tumours that result from malignant transformation are SCCs. Other subtypes include adenocarcinomas, small cell carcinomas, sarcomas, thyroid carcinomas, malignant melanomas, and neuroectodermal tumours (Atwi et al, 2022). The most common signs and symptoms of SCC transformation in MCT of the ovary were abdominal pain (47.3%) and an abdominal mass (26.0%) (Li et al, 2019).

Hypercalcaemia has been associated with 5% of gynaecologic malignancies. Clear cell ovarian carcinoma is the most common ovarian subtype associated with this electrolyte imbalance (Agarwal et al, 2013). There are only a few case reports in the literature that

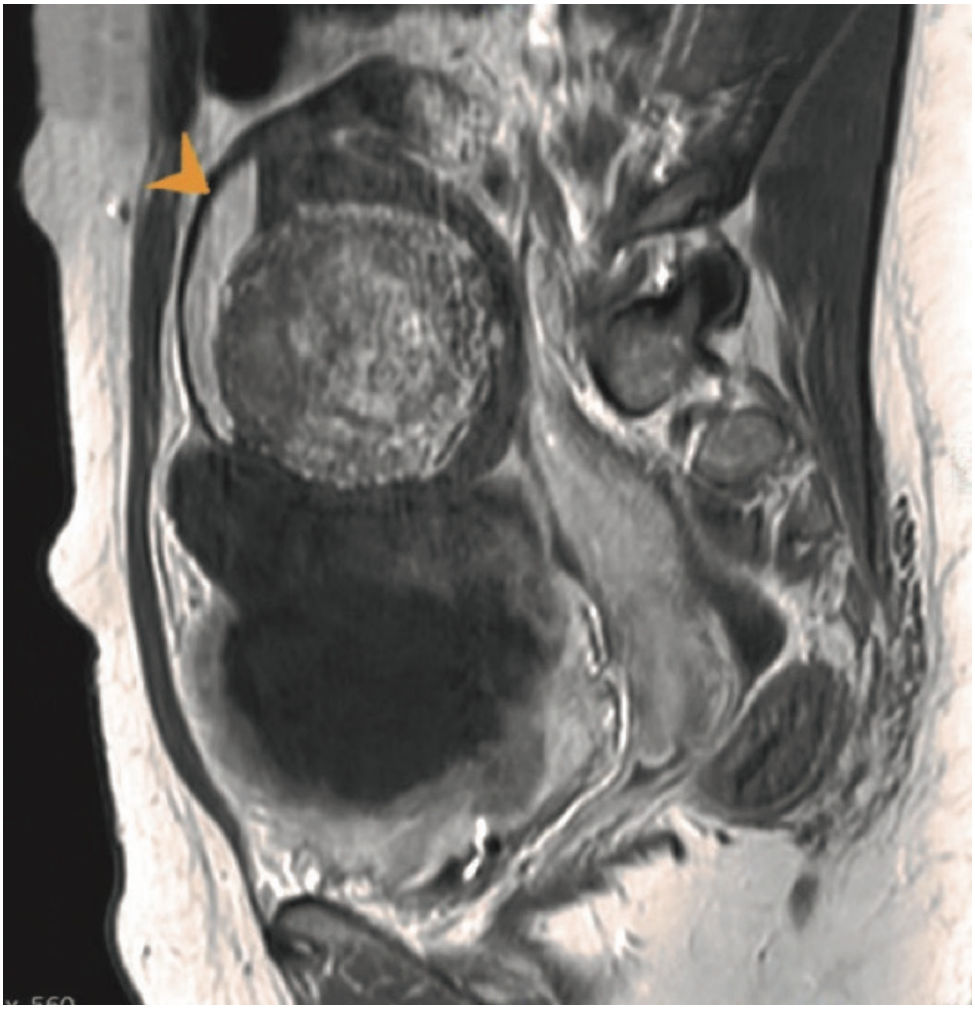

Figure 2. Saggital view of MR pelvis showing pelvic mass (arrow pointing to the superior aspect of a mass lesion).

Table 1. Blood investigations

Investigation	Results	Range
Creatinine	57	45–84 umol/L
Estimated glomerular filtration rate	108	mL/min/1.73 m^2
Calcium	2.69	2.15–2.55 mmol/L
Phosphate	1.08	0.87–1.45 mmol/L
Corrected calcium	2.67	2.05–2.6 mmol/L
Parathyroid hormone-related protein	1.8	range: <1.30 pmol/L
Parathyroid hormone	<0.5	range: 1.96–9.33 pmol/L
Angiotensin converting enzyme level	59.99	20–70 u/L
Serum protein electrophoresis	no monoclonal band detected	
25 OH vitamin D	<13 ng/mL	30–100
1,25-dihydroxyvitamin D	110	47.04–130 pmol/L

describe hypercalcaemia associated with an SCC arising in an MCT (Ribeiro et al, 1988; Takeuchi et al, 2000).

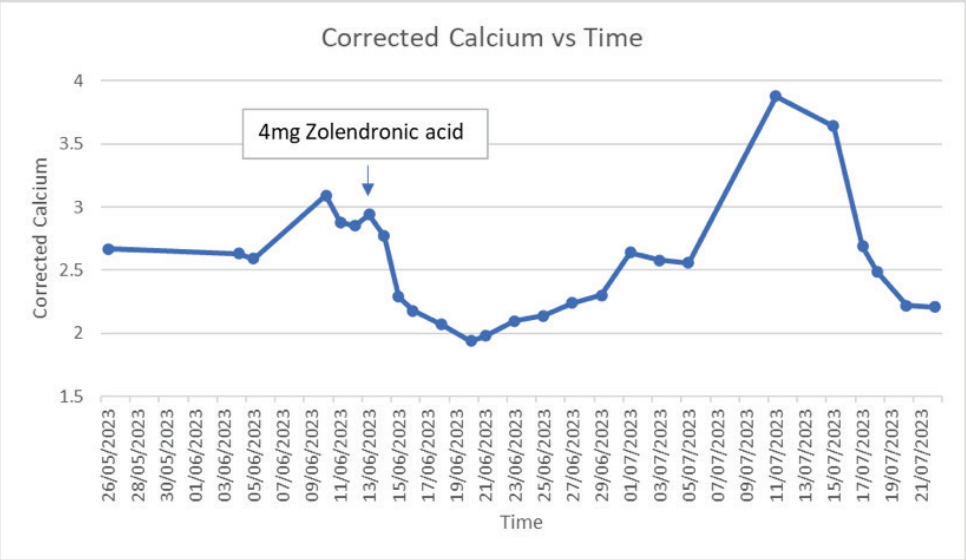

Figure 3. Graph showing the variation of corrected calcium level vs time.

The three major causes of hypercalcaemia include tumour secretion of parathyroid hormone-related protein (PTHrP), osteolytic metastases, and tumour production of 1,25-dihydroxyvitamin D (calcitriol). Complete surgical removal of the tumour is the treatment of choice to treat humoral hypercalcaemia of malignancy (HHM).

Intravenous fluids increase calcium excretion and bisphosphonates are the mainstay of therapy. They inhibit the apoptosis of osteoblasts and induce the apoptosis of osteoclasts but their effect on serum calcium only lasts 3–4 weeks. In fact, our patients' calcium increased again after three weeks. Other options to treat HHM include calcitonin and denosumab. Calcitonin decreases the resorption of hydroxyapatite from bone and enhances the renal excretion of calcium. Denosumab is a RANKL antibody that inhibits osteoclast maturation, activation, and function (Asonitis et al, 2019).

Learning points

- Our case highlights two important lessons to keep in mind regarding SCCs arising from MCTs; they can occur in younger women, and may be associated with severe hypercalcaemia.
- Preoperatively, tumour size, age and tumour markers may increase suspicion of malignant transformation (Atwi et al, 2022). High concentrations of squamous cell carcinoma antigen (SCC Ag), CA-125, CA 19-9, CEA, and AFP have been associated with malignant transformation.
- Some features on preoperative CT and MRI such as solid tissue components extending through the wall and invading adjacent structures are strongly suggestive of malignant transformation (Atwi et al, 2022) but imaging is not always helpful. For example, in our case imaging initially suggested that the left ovarian cyst had undergone malignant transformation but histologically this had occurred within the right ovary.
- A definitive diagnosis of malignant transformation of an MCT can only be made histologically.

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Availability of data and materials

All the data of this study are included in this article.

Author contributions

AM, NM, MG, AC and KMVB designed the research study. AM, NM and MG analyzed the data. NM drafted the manuscript. All authors contributed to important editorial changes in the manuscript. All authors read and approved the final manuscript. All authors have participated sufficiently in the work and agreed to be accountable for all aspects of the work.

Ethics approval and consent to participate

The participant signed an informed consent form.

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Conflict of interest

The authors declare no conflict of interest.

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